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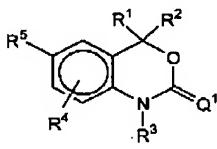
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (Currently Amended). A method of inducing contraception comprising the step of delivering to a female of child-bearing age a composition comprising a compound of formula I or formula II, or a tautomer thereof, in a regimen which involves delivering a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to said female,

wherein formula I is:



I

wherein:

R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, substituted C₂ to C₆ alkynyl, C₃ to C₈ cycloalkyl, phenyl, and thiophene substituted C₃ to C₈ cycloalkyl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^A, and NR^BCOR^A;

or R¹ and R² are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C₁ to C₆ alkyl;

a) a carbon-based 3 to 8 membered saturated spirocyclic ring;

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b) — a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and

c) — a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

R^A is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₄ to C₆ alkoxy, substituted C₄ to C₆ alkoxy, amino, C₄ to C₆ aminoalkyl, and substituted C₄ to C₆ aminoalkyl;

R^B is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

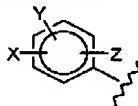
R^3 is selected from the group consisting of H, OH, NH₂, C₁ to C₆ alkyl, substituted C₄ to C₆ alkyl, C₄ to C₆ alkenyl, substituted C₄ to C₆ alkenyl, alkenyl, substituted alkenyl, and COR^C;

R^6 is selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, aryl, substituted aryl, C₄ to C₆ alkoxy, substituted C₄ to C₆ alkoxy, C₄ to C₆ aminoalkyl, and substituted C₄ to C₆ aminoalkyl;

R^4 is selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₄ to C₆ alkoxy, substituted C₄ to C₆ alkoxy, C₄ to C₆ aminoalkyl, and substituted C₄ to C₆ aminoalkyl;

R^5 is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, C₄ to C₆ aminoalkyl, substituted C₄ to C₆ aminoalkyl, NO₂, and C₁ to C₃ perfluoroalkyl, substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms;

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substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^9 , OCOR^9 , and NR^6COR^9 ;

R^9 is selected from the group consisting of H, C_1 to C_2 alkyl, substituted C_1 to C_2 alkyl, aryl, substituted aryl, C_1 to C_2 alkoxy, substituted C_1 to C_2 alkoxy, C_1 to C_2 aminoalkyl, and substituted C_1 to C_2 aminoalkyl;

R^6 is selected from the group consisting of H, C_1 to C_3 alkyl, and substituted C_1 to C_3 alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO_2 , C_1 to C_3 alkoxy, substituted C_1 to C_3 alkoxy, C_1 to C_4 alkyl, and substituted C_1 to C_4 alkyl, C_1 to C_3 thioalkyl, and substituted C_1 to C_3 thioalkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms heteroatom selected from the group consisting of O, S, SO , SO_2 , and NR^6 and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO_2 , C_1 to C_4 alkyl, and substituted C_1 to C_4 alkyl, C_1 to C_2 alkoxy, substituted C_1 to C_2 alkoxy, C_1 to C_3 aminoalkyl, substituted C_1 to C_3 aminoalkyl, C_1 to C_3 perfluoroalkyl, substituted C_1 to C_3 perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C_1 to C_2 thioalkyl, substituted C_1 to C_2 thioalkyl, COR^F , and NR^6COR^F ;

R^F is selected from the group consisting of H, C_1 to C_3 alkyl, substituted C_1 to C_2 alkyl, aryl, substituted aryl, C_1 to C_2 alkoxy, substituted C_1 to C_2 alkoxy, C_1 to C_2 aminoalkyl, and substituted C_1 to C_2 aminoalkyl;

R^G is selected from the group consisting of H, C_1 to C_3 alkyl, and substituted C_1 to C_3 alkyl;

R^6 is selected from the group consisting of H, C_1 to C_3 alkyl, and C_1 to C_4 CO_2 alkyl;

Q^1 is selected from the group consisting of S, NR^7 , and CR^8R^9 ;

R^7 is selected from the group consisting of CN, C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_2 to C_6 cycloalkyl, substituted C_2 to C_6 cycloalkyl, aryl, substituted aryl,

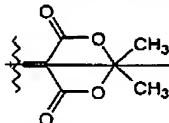
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carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO_2CF_3 , OR^{11} , and $\text{NR}^{11}\text{R}^{12}$;

R^8 and R^9 are independent substituents selected from the group consisting of H, C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, C_3 to C_8 cycloalkyl, substituted C_3 to C_8 cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO_2 , CN , and CO_2R^{10} ;

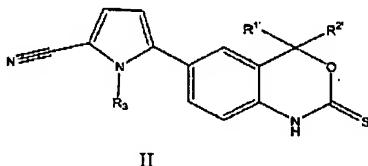
R^{10} is selected from the group consisting of C_1 to C_3 alkyl and substituted C_1 to C_3 alkyl;

or CR^8R^9 comprise a six membered ring having the structure:



R^{11} and R^{12} are independently selected from the group consisting of H, C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



wherein:

R^{11} is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R^{12} is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

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R^1 and R^2 are joined to form a spirocyclic ring containing 3 to 7 carbon atoms; and R^3 is selected from the group consisting of C_1 to C_4 alkyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II.

2(Original). The method according to claim 1, wherein said compound of formula I or formula II and said selective estrogen receptor modulator are delivered in a single composition.

3(Original). The method according to claim 1, wherein said compound of formula I or formula II and said selective estrogen receptor modulator are delivered separately.

4(Original). The method according to claim 1, wherein said selective estrogen receptor modulator is selected from the group consisting of EM-800, EM-652, raloxifene hydrochloride, arzoxifene, lasofoxifene, droloxifene, idoxifene, levormeloxifene, centchroman, nafoxidene, tamoxifen citrate, 4-hydroxytamoxifen citrate, clomiphene citrate, toremifene citrate, pipendoxifene, and bazedoxifene.

5(Original). The method according to claim 1, wherein said compound is delivered at a daily dosage of about 0.1 to about 50 mg.

6(Original). The method according to claim 1, wherein said regimen comprises delivering said composition daily for 1 to about 21 days, wherein said regimen is a cycle which is repeated monthly.

7(Original). The method according to claim 1, wherein said selective estrogen receptor modulator is delivered at a daily dosage of about 0.2 to about 100 mg.

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8(Currently Amended). The method according to Claim 1, wherein in formula I:

R^1 is selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ cycloalkyl, substituted C₃ to C₆ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR⁴, and NR⁵COR⁴;

R^2 is selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, C₂ to C₆ cycloalkyl, substituted C₂ to C₆ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR⁴, and NR⁵COR⁴;

R^4 is selected from the group consisting of H, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, aryl, substituted aryl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ aminoalkyl, and substituted C₁ to C₃ aminoalkyl;

R^5 is selected from the group consisting of (iii) and (iv).

(iii) the substituted benzene ring, wherein:

X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, C₁ to C₃ aminoalkyl, substituted C₁ to C₃ aminoalkyl, NO₂, C₁ to C₃ perfluoroalkyl, 5 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR⁶, OCOR⁶, and NR⁶COR⁶; and

(iv) the five or six membered ring, wherein said one or two independent substituents are selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₃ alkyl, and C₁ to C₃ alkoxy;

R^7 is selected from the group consisting of CN, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ cycloalkyl, substituted C₃ to C₆ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, and SO₂CF₃,

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9(Currently Amended). The method according to claim 8, wherein in formula I:

R^1 and R^2 are independently selected from the group consisting of C_1 to C_3 alkyl and substituted C_1 to C_3 alkyl;

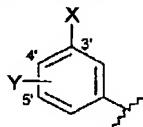
or R^1 and R^2 are fused to form the carbon-based 3 to 6 membered saturated spirocyclic ring;

R^3 is selected from the group consisting of H, OH, NH_2 , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, and COR^6 ;

R^6 is selected from the group consisting of H, C_1 to C_4 alkyl, and C_1 to C_4 alkoxy;

R^4 is selected from the group consisting of H, halogen, NO_2 , C_1 to C_3 alkyl, and substituted C_1 to C_3 alkyl;

R^5 is the substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN , C_1 to C_3 alkoxy, C_1 to C_3 alkyl, NO_2 , and C_1 to C_3 perfluoroalkyl, 5 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, and C_1 to C_3 thioalkyl.

10(Currently Amended). The method according to Claim 8, wherein in formula I:

R^1 and R^2 are independently selected from the group consisting of C_1 to C_3 alkyl and substituted C_1 to C_3 alkyl;

or R^1 and R^2 are fused to form the carbon-based 3 to 6 membered saturated spirocyclic ring;

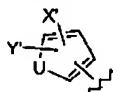
R^3 is selected from the group consisting of H, OH, NH_2 , C_1 to C_6 alkyl, substituted C_1 to C_6 alkyl, and COR^6 ;

R^6 is selected from the group consisting of H, C_1 to C_4 alkyl, and C_1 to C_4 alkoxy;

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R^4 is selected from the group consisting of H, halogen, NO_2 , C_1 to C_3 alkyl, and substituted C_1 to C_3 alkyl;

R^5 is the five membered ring having the structure:



U is selected from the group consisting of O, S, and NR^5NR^6 ;

X' is selected from the group consisting of halogen, CN, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl, NO_2 , C_4 to C_7 perfluoroalkyl, 5 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, and C_4 to C_7 thiealkyl;

Y' is selected from the group consisting of H, halogen, CN, NO_2 , C_1 to C_3 alkoxy, and C_1 to C_3 alkyl, and C_4 to C_7 thiealkyl.

11 (Currently Amended). The method according to claim 8, wherein in formula I:

R^1 and R^2 are independently selected from the group consisting of C_1 to C_3 alkyl and substituted C_1 to C_3 alkyl;

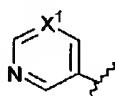
or R^4 and R^2 are fused to form the carbon-based 3 to 6 membered saturated spirocyclic ring;

R^4 is selected from the group consisting of H, OH, NH_2 , C_1 to C_3 alkyl, substituted C_1 to C_3 alkyl, and COR^6 ;

R^6 is selected from the group consisting of H, C_4 to C_7 alkyl, and C_1 to C_4 alkoxy;

R^4 is selected from the group consisting of H, halogen, NO_2 , C_1 to C_3 alkyl, and substituted C_1 to C_3 alkyl;

R^5 is the six membered ring having the structure:



X^1 is selected from the group consisting of N and CX^2 ;

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X^2 is selected from the group consisting of halogen, and CN, and NO₂.

12-13(Canceled).

14(Original). The method according to claim 1, wherein in formula I: R¹ and R² are fused to form a carbon-based 3 to 6 membered saturated spirocyclic ring.

15-24(Canceled).

25(Original). The method according to claim 1 wherein said compound of formula I is selected from the group consisting of 6-(3-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-benzo[d][1,3]oxazin-2-thione, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-thiophene-2-carbonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-benzonitrile, 6-(3-fluorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-methylthiophene-2-carbonitrile, tert-Butyl 2-cyano-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-1-carboxylate, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbonitrile, [6-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-pyridin-2-yl]acetonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbothiamide, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-thiophene-3-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-ethyl-1H-pyrrole-2-carbonitrile, 4-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-fluorobenzonitrile, 6-(5-Bromopyridin-3-yl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chloro-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-methylphenyl)-4,4-dimethyl-1,4-

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dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-trifluoromethoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(1,2-Dihydro-2-thioxo spiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methylbenzonitrile, 6-(3,5-Dichlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-1,2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)isophthalonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4,4-Diethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4-methyl-4-phenyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Allyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-Chloro-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 6-(3,5-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Fluoro-5-methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methoxybenzonitrile, 6-(3-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3,4-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(4-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-fluorobenzonitrile, 6-(2,3-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(8-Bromo-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-fluorobenzonitrile, 4,4-Dimethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4,4-diethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Benzyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-2-carbonitrile, 3-Fluoro-5-(8-fluoro-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-

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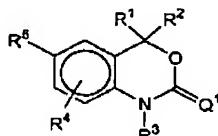
3,1-benzoxazin-6-yl)benzonitrile, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)benzonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-4-methyl-2-thiophenecarbonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 6-(3-Chloro-4-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-propylthiophene-2-carbonitrile, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4-Butyl-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-2-carbonitrile, 6-(3-Bromophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, and 2-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-3-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

26(Original). The method according to claim 1, wherein said compound of formula I is 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

27(Original). The method according to claim 1, wherein said compound of formula II is selected from the group consisting of: 5-(4-ethyl-4-methyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-diethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclohexan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclopentan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-[2-thioxo-4,4-bis(trifluoromethyl)-1,4-dihydro-2H-3,1-benzoxazine-6-yl]-1H-pyrrole-2-carbonitrile, and prodrugs, metabolites, and pharmaceutically acceptable salts thereof.

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28(Currently Amended). A pharmaceutical kit useful for inducing contraception or hormone replacement therapy, said kit comprising a compound of formula I or formula II and at least one selective estrogen receptor modulator, wherein formula I is:



I

wherein:

R¹ and R² are independent substituents selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₂ to C₆ alkenyl, substituted C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, substituted C₂ to C₆ alkynyl, C₃ to C₈ cycloalkyl, phenyl, and thiophene substituted C₁ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^A, and NR^BCOR^A;

or R¹ and R² are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C₁ to C₆ alkyl;

- a) a carbon-based 3 to 8 membered saturated spirocyclic ring;
- b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and
- c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

R^A is selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, aryl, substituted aryl, C₁ to C₆ alkoxy, substituted C₁ to C₆ alkoxy, amino, C₁ to C₆ aminoalkyl, and substituted C₁ to C₆ aminoalkyl;

R^B is selected from the group consisting of H, C₁ to C₆ alkyl, and substituted C₁ to C₆ alkyl;

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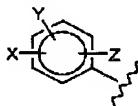
R^3 is selected from the group consisting of H, OH, NH₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₆ alkenyl, substituted C₁ to C₆ alkenyl, alkenyl, substituted alkenyl, and COR^C;

R^C is selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, aryl, substituted aryl, C₁ to C₄ alkoxy, substituted C₁ to C₄ alkoxy, C₁ to C₄ aminealkyl, and substituted C₁ to C₄ aminealkyl;

R^4 is selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, C₁ to C₆ alkoxy, substituted C₁ to C₆ alkoxy, C₁ to C₆ aminealkyl, and substituted C₁ to C₆ aminealkyl;

R^5 is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C₁ to C₃ alkyl, substituted C₁ to C₃ alkyl, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₃ thioalkyl, substituted C₁ to C₃ thioalkyl, C₁ to C₃ aminealkyl, substituted C₁ to C₃ aminealkyl, NO₂, and C₁ to C₃ perfluoroalkyl; substituted C₁ to C₃ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR^B, OCOR^B, and NR^BCOR^B;

R^B is selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, aryl, substituted aryl, C₁ to C₆ alkoxy, substituted C₁ to C₆ alkoxy, C₁ to C₆ aminealkyl, and substituted C₁ to C₆ aminealkyl;

R^6 is selected from the group consisting of H, C₁ to C₃ alkyl, and substituted C₁ to C₃ alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₃ alkoxy, substituted C₁ to C₃ alkoxy, C₁ to C₄ alkyl, and substituted C₁ to C₄ alkyl, C₁ to C₃ thioalkyl, and substituted C₁ to C₃ thioalkyl; and

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(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms heteroatom selected from the group consisting of O, S, SO, SO₂, and NR⁶ and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO₂, C₁ to C₄ alkyl, and substituted C₁ to C₄ alkyl, C₁ to C₄ alkoxy, substituted C₁ to C₄ alkoxy, C₁ to C₄ aminoalkyl, substituted C₁ to C₄ aminoalkyl, C₁ to C₄ perfluoroalkyl, substituted C₁ to C₄ perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C₁ to C₄ thioalkyl, substituted C₁ to C₄ thioalkyl, COR⁵, and NR⁶COR⁵;

R⁵ is selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, aryl, substituted aryl, C₁ to C₄ alkoxy, substituted C₁ to C₄ alkoxy, C₁ to C₄ aminoalkyl, and substituted C₁ to C₄ aminoalkyl;

R⁶ is selected from the group consisting of H, C₁ to C₄ alkyl, and substituted C₁ to C₄ alkyl;

R⁶ is selected from the group consisting of H, C₁ to C₄ alkyl, and C₁ to C₄ CO₂alkyl;

Q¹ is selected from the group consisting of S, NR⁷, and CR⁸R⁹;

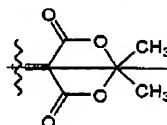
R⁷ is selected from the group consisting of CN, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₂ to C₈ cycloalkyl, substituted C₂ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO₂CF₃, OR¹¹, and NR¹²R¹³;

R⁸ and R⁹ are independent substituents selected from the group consisting of H, C₁ to C₄ alkyl, substituted C₁ to C₄ alkyl, C₂ to C₈ cycloalkyl, substituted C₂ to C₈ cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO₂, CN, and CO₂R¹⁰;

R¹⁰ is selected from the group consisting of C₁ to C₄ alkyl and substituted C₁ to C₄ alkyl;

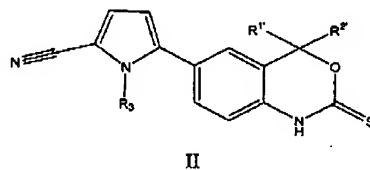
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or CR^8R^9 comprise a six membered ring having the structure:



R^{11} and R^{12} are independently selected from the group consisting of H, C₁ to C₆ alkyl, substituted C₁ to C₆ alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



wherein:

R^{11} is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R^{12} is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R^{11} and R^{12} are joined to form a spirocyclic ring containing 3 to 7 carbon atoms; and $\text{R}^{3'}$ is C₁ to C₄ alkyl; and

a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.